The Determination of the Absolute Configuration of (−)-Kopsanone

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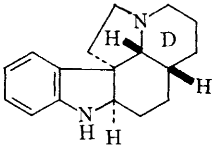
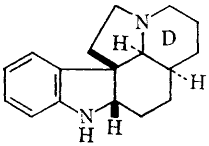
THERE are two naturally occurring series of *Aspidosperma* alkaloids which differ in that their skeletal structures (Ia) and (Ib) are optical antipodes. Thus (+)-aspidospermidine, (−)-aspidospermine† and (−)-pyrifolidine belong to series (Ia) and (+)-pyrifolidine belongs to series (Ib). It has been suggested[1] that these series arise from a non-asymmetric intermediate in *Aspidosperma* alkaloid biosynthesis.

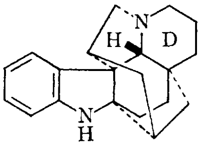
The structures and relative stereochemistry of a number of *Kopsia* alkaloids are known[2,3] from their chemical relationships and from n.m.r. and mass-spectral data. Although the kopsane skeleton is similar to the aspidospermine skeleton and may also adopt either the configuration (IIa) or (IIb), it appears that the presently known *Kopsia* alkaloids belong to the same antipodal series, with the possible exception of kopsine.‡ Conflicting enantiomeric formulations (IIa) and (IIb) have been reported. The kopsane skeleton was first assumed



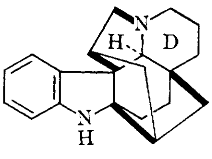
(Ia)



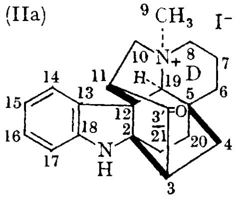
(Ib)



(IIa)



(IIb)



(III)

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† A recent determination of the absolute configuration of (−)-aspidospermine *N*(b)-methiodide by B. M. Craven and D. E. Zacharias (unpublished) using the *X*-ray dispersion effect has confirmed the skeletal structure as (Ia).

‡ Specific rotations $[\alpha]_D^{20}$ of opposite sign have been reported for kopsine (+16·4° in ethyl alcohol[5] and −17·5° in chloroform[6]). It is not clear whether this is the result of a solvent effect or of enantiomerism.

to have the configuration (IIa), by analogy with (—)-aspidospermine and because four *Kopsia* alkaloids, including kopsanone, have been isolated from two species of *Aspidosperma* (*A. Duckei* Hub. and *A. Macrocarpon* Mast.).[2] Soon after, the opposite assignment (IIb) was made on the basis of a chemical correlation with minovincine.[3]

We now establish the absolute configuration of (—)-kopsanone and related alkaloids by X-ray crystal structure determination of the N(b)-methiodide (Figure), showing that this corresponds to (IIb). The crystals of kopsanone N(b)-methiodide are orthorhombic, a = 13·98, b = 17·20, and c = 7·67 Å with space group $P2_12_12_1$, and four molecules per cell. The three dimensional X-ray intensity data (1800 reflections) were collected using an automatic four-circle diffractometer and Cu-K_α radiation. The structure determination was by the heavy-atom method followed by least-squares refinement of positional and individual isotropic thermal parameters for all atoms, including iodine. The refinement procedure, assuming anomalously X-ray scattering iodine atoms, converged at R = 0·11 for the (IIa)-type structure and R = 0·08 for the (IIb)-type structure. The (IIb) configuration was confirmed by the measurement of $\bar{h}\bar{k}\bar{l}$ intensities for the three strong reflections 111, 133, 912. For these the calculated values of $(I_{hkl}-I_{\bar{h}\bar{k}\bar{l}})/I_{hkl}$ based on the (IIb) configuration are +0·27, —0·17, +0·02 and the corresponding observed values are +0·22, —0·25, +0·02.

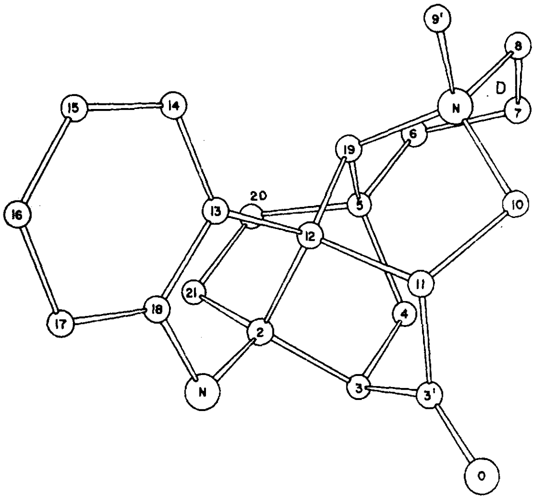

FIGURE. *Kopsanone* N(*b*)-*methiodide*

The X-ray results confirm the relative stereochemistry (III) previously deduced for (—)-kopsanone, the only new feature being the *chair* conformation of ring D (Figure). In crystal structure determinations of alkaloids containing the aspidospermine skeleton (I),[4] it has been shown that ring D is consistently in the *boat* conformation.

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